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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/039,761	10/19/2001	Brian Wong	021044-007310US	9200

20350 7590 03/08/2005

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EXAMINER

MURPHY, JOSEPH F

ART UNIT PAPER NUMBER

1646

DATE MAILED: 03/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

10/039,761

Applicant(s)

WONG ET AL.

Examiner

Joseph F Murphy

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 1/11/2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-27 is/are pending in the application.
- 4a) Of the above claim(s) 6-10, 16-27 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5 and 11-15 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |   |   |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)  | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>01112005</u> . | 6) <input type="checkbox"/> Other: _____  |

## **DETAILED ACTION**

### ***Formal Matters***

Claims 1-27 are pending. Claims 1-5, 11-15 are under consideration. Claims 6-10, 16-27 stand withdrawn from consideration pursuant to 37 CFR 1.142(b).

### ***Response to Amendment***

The Declaration filed on 12/16/2004 under 37 CFR 1.131 is sufficient to overcome the WO 0078934 (Nizetic et al.) reference.

The objection to claims 1-5, 11-15 has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues are set forth below.

### ***Claim Rejections - 35 USC § 112 first paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 11-15 stand rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for methods of identification of agents capable of modulating the activity of a protein 95% identical to the USP-25 protein, with the sequence as set forth in SEQ ID NO: 2, wherein the assay uses a target protein fused with ubiquitin and further wherein the target protein is UBC9, SYK or calcineurin, and further wherein the ubiquitin like protein is SMT3/SUMO, NEDD8/RUBY, does not reasonably provide enablement for methods of identification of agents capable of modulating the activity of a protein 95% identical to the USP-25 protein, with the sequence as set forth in SEQ ID NO: 2, wherein the assay uses a target protein fused with ubiquitin, for reasons of record set forth in the Office Action of 6/11/2004.

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The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to for methods of identification of agents capable of modulating the activity of a protein 95% identical to the USP-25 protein, with the sequence as set forth in SEQ ID NO: 2, wherein the assay uses a target protein fused with ubiquitin. Claims 1, 5, 11, 15 are overly broad since insufficient guidance is provided as to which protein will serve as a target for USP-25. The claims are directed to methods using variant polypeptides, while the Specification only teaches the use of target proteins comprising UBC9, SYK or calcineurin, and wherein the ubiquitin like protein is SMT3/SUMO, NEDD8/RUBY. Since the claims encompass variant polypeptides and given the unpredictability of the effect of variations on protein function, it would require undue experimentation to practice the claimed invention. See *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the target polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to practice the claimed invention, while the claims encompass target polypeptides which the specification only

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teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to practice the claimed invention.

Applicant argues that one of skill in the art would know how to avoid the inoperative embodiments and to identify USP-25 target proteins without undue experimentation, and that the application provides guidance in the form of assays and working examples for identification of USP-25 target proteins. However, the claims are directed to a method of screening for an agent which modulates USP-25 protein activity, while the term protein activity is unclear, as set forth in the rejection under 35 USC 112 second paragraph set forth *infra*. The nexus between the USP-25 target protein and the protein activity of USP-25 which is to be modulated by the identified agent is not clear. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides, since the skilled artisan would have to first determine the target USP-25 polypeptide, then determine a protein activity which is to be modulated, then carry out the method.

Claims 1-5, 11-15 stand rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for reasons of record set forth in the Office Action of

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6/11/2004. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to for methods of identification of agents capable of modulating the activity of a protein 95% identical to the USP-25 protein, with the sequence as set forth in SEQ ID NO: 2, wherein the assay uses a target protein fused with ubiquitin. These are genus claims because the claims are thus directed to methods using variant polypeptides. The specification and claim do not indicate what distinguishing attributes shared by the members of the genus. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the use of target proteins comprising UBC9, SYK or calcineurin, and the ubiquitin like proteins SMT3/SUMO, NEDD8/RUBY is insufficient to describe the genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions that are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and

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there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the target polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Applicant argues that the application provides support for the full concept of the claimed genus, and that assays used to identify USP-25 target proteins used in the claimed methods were well known at the time of filing and the descriptions provided easily meet the properly applied standard of written description. However, the claims are directed to a method of screening for an agent which modulates USP-25 protein activity, while the term protein activity is unclear, as set forth in the rejection under 35 USC 112 second paragraph set forth *infra*. The nexus between the USP-25 target protein and the protein activity of USP-25 which is to be modulated by the identified agent is not clear. However, the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant

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was in possession of the claimed genus. In the instant case, there is not a correlation between the USP-25 target protein which needs to be determined by the skilled artisan, since the structure is not set forth in the claim, and the USP-25 protein activity, which is indefinite.

***Claim Rejections - 35 USC § 112 second paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-5, 11-15 stand rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for reasons of record set forth in the Office Action of 6/11/2004.

Claims 1 and 11 are vague and indefinite in the recitation of the term "protein activity". The term " protein activity " is not defined by the claim, but give no definition of what this activity is. Various biological activities can be attributed to a peptide. For example, "activity" could constitute transportation throughout a cell, alteration of tertiary structure due to changes in pH, ligand binding, or modulation of second messenger effect, etc. 'Activity' could also be referring to the ability of the fragment to stimulate antibody production. Claims 2-5, 12-15 are rejected insofar as they depend on the recitation on claims 1 and 11 of "protein activity".

Applicant argues that the claims clearly refer to USP-25 protein activity, which is clearly defined in the specification at page 45, lines 11-24. USP-25 protein activity includes, e.g., "modulation of ' leukocyte activation', modulation of platelet activation; modulation of lymphocyte activation;" etc. However, although the claims are interpreted in light of the



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specification, limitations from the specification are not read into the claims. In re Van Geuns, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Applicant is attempting to read these limitations into the claim, which is improper. In reviewing a claim for compliance with 35 U.S.C. 112, second paragraph, the examiner must consider the claim as a whole to determine whether the claim appraises one of ordinary skill in the art of its scope and, therefore, serves the notice function required by 35 U.S.C. 112, second paragraph “by providing clear warning to others as to what constitutes infringement of the patent”. See, e.g., *Solomon v. Kimberly-Clark Corp.*, 216 F.3d 1372, 1379, 55 USPQ2d 1279, 1283 (Fed. Cir. 2000). MPEP 2173.02, MPEP 2173.02. In the instant case, various activities can be attributed to a protein, and it is an insufficient indication to the skilled artisan of the metes and bounds of the claims to list several exemplary functions in the specification to attempt to define the term.

### ***Conclusion***

No claim is allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

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CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.  
Patent Examiner  
Art Unit 1646  
February 28, 2005

  
JOSEPH MURPHY  
PATENT EXAMINER